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Literature Review

4DCT radiotherapy for NSCLC: a review of planning methods

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Abstract

Purpose: To establish whether the use of a passive or active technique of planning target volume (PTV) definition and treatment methods for non-small cell lung cancer (NSCLC) deliver the most effective results. This literature review assesses the advantages and disadvantages in recent studies of each, while assessing the validity of the two approaches for planning and treatment.

Methods: A systematic review of literature focusing on the planning and treatment of radiation therapy to NSCLC tumours. Different approaches which have been published in recent articles are subjected to critical appraisal in order to determine their relative efficacy.

Results: Free-breathing (FB) is the optimal method to perform planning scans for patients and departments, as it involves no significant increase in cost, workload or education. Maximum intensity projection (MIP) is the fastest form of delineation, however it is noted to be less accurate than the ten-phase overlap approach for computed tomography (CT). Although gating has proven to reduce margins and facilitate sparing of organs at risk, treatment times can be longer and planning time can be as much as 15 times higher for intensity modulated radiation therapy (IMRT). This raises issues with patient comfort and stabilisation, impacting on the chance of geometric miss. Stereotactic treatments can take up to 3 hours to treat, along with increases in planning and treatment, as well as the additional hardware, software and training required.

Conclusion: Four-dimensional computed tomography (4DCT) is superior to 3DCT, with the passive FB approach for PTV delineation and treatment optimal. Departments should use a combination of MIP with visual confirmation ensuring coverage for stage 1 disease. Stages 2–3 should be delineated using ten-phases overlaid. Stereotactic and gated treatments for early stage disease should be used accordingly; FB-IMRT is optimal for latter stage disease.

Keywords: computed tomography (CT); delineation; four-dimensional computed tomography (4DCT); free-breathing; gated; internal target volume (ITV); lung cancer; non-small cell lung cancer (NSCLC); planning target volume (PTV); radiotherapy; radiotherapy planning

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INTRODUCTION

Lung cancer is responsible for ~7,600 deaths annually and over 10,000 diagnoses per year in Australia.[1] Non-small cell lung cancer (NSCLC) is responsible for up to 85% of lung cancers, with a 5 year survival rate of ~10–20% using 3D conformal radiation therapy (3DCRT). Treatment options commonly available to patients include surgery, chemotherapy and radiation therapy. However, due to the age and co-morbidities of the majority of patients, surgery is commonly not performed. Chemotherapy has also shown an increase in toxicities with little improvement to local control.[2] However, technologies such as intensity modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT) and four-dimensional computed tomography (4DCT) are showing promise in improving these rates; as high as 47% for 5-year survival.[3]

There are several methods commonly used for delineation of target volumes for NSCLC patients. For IMRT, SBRT and gated treatments the need for accurate delineation is paramount. The free-breathing (FB) 4DCT scans can be viewed individually, forming ten separate scans that are delineated separately. Breath-hold techniques can be used to form datasets of end-inspiration and end-expiration to compare the extent of motion at either end of the respiratory cycle. Maximum intensity projection (MIP) uses the maximum voxel intensities across all phases of the patient's breathing cycle to form a single scan with a volume accounting for the entirety of motion.[2] Average intensity (AI) performs a similar method whereby it allocates the AI voxels to form a volume.[2,4] Each of these methods has advantages and disadvantages which will be reviewed in this paper.

The accuracy of delineation is increased when using multiple stages of the breathing cycle: from inhalation to mid ventilation or from mid ventilation to exhalation. This accounts for differences throughout the breathing cycle and also illustrates the overall displacement in three dimensions.[5] Methods of 4DCT essentially form an oversampled 3DCT scan, which can be separated into phases of the breathing cycle to determine time-specific target positions. The planning scan is performed with the patient in the treatment position, under natural FB conditions in the majority of cases.[6]

Planning target volume (PTV) delineation for NSCLC patients can be performed in two definitive ways using 4D technology. The first is to use computed tomography (CT) data to depict the extent of motion of the target and incorporate this motion as part of the PTV (internal target volume (ITV)), increasing the accuracy of treating the structure, thus tumour control probability (TCP), but increasing normal tissue dose and normal tissue complication probability (NTCP). This is deemed a 'passive' approach, as the treatment of the patient is delivered under the same FB circumstances as a 3DCRT plan. The alternative is to use tracking systems and/or gating methods to acquire CT data and treat a reduced volume while increasing the likelihood of treating the target during a specific respiratory stage. This is an 'active' approach and has the potential to escalate dose to the target and minimise normal tissue dose, increasing TCP. Active methods rely on significant stabilisation and imaging equipment to negate geometric miss.[7,8]

Unfortunately, conventional CT images of lung tumours generate artefacts and blurring of the internal anatomy due to the stacking of images with no perception of time.[9] Helical CT commonly used for planning purposes, forms only a snapshot of the tumour position during differing phases of the respiratory cycle. Artefacts and degradation of the volume is common in 3D scans, increasing geometric uncertainties. These are commonly accounted for by the internal (IM) and set up (SM) margins within radiotherapy treatments. The IM consists of the displacement the target experiences throughout the entire breathing cycle, forming the ITV.[7] Although the ITV increases geometric accuracy, the increase in normal tissue and critical structure dose significantly reduces patient quality of life.[6]

An innovative method designed to account for respiratory motion is 4DCT. By increasing the scan time and decreasing pitch (movement rate of the CT couch) the breathing cycle and

subsequent position of the target volume can be viewed across ten discrete phases.[8] This provides temporal and spatial information critical to reducing geometric uncertainties for accurate delineation of target volumes across the breathing cycle.[4,10] 4DCT has created opportunities to treat patients with SBRT, IMRT and gating techniques.[8,11]

There are multiple technologies available to monitor breathing patterns of patients, including active breathing control (ABC) and real-time position management (RPM).[12] The latter tracking system utilises external markers with infra-red technology to monitor their displacement. Due to the complications and co-morbidities exhibited by many lung patients, external markers are more suitable and are less invasive than internal markers, which some systems can use.[8]

Limitations with conventional treatment occur due to the sensitivity of organs such as lungs, whereby late toxicities from extensive low-dose to large volumes of organ reduce the likelihood of escalating dose. IMRT is designed to treat complex volumes, avoiding organs at risk (OAR) and thus allow for dose escalation to target volumes. Unlike conventional planning, the V20 lung dose can be within tolerance, however the V5 or V20 volumes can be much larger (as high as 50%) compared with the lower doses achieved in 3DCRT. Additionally, two other factors are crucial to the use of IMRT as an accurate alternative: tumour motion and target delineation. Due to the complexity of IMRT and the use of dynamic MLCs, the effects of target-miss are emphasised, therefore a method to account for these is required.[13]

Recent literature demonstrates that FB during IMRT treatments proves insignificant to the dose distribution changes between planning system and treatment. This strengthens the validity for FB 4DCT techniques to be used in the planning of NSCLC patients, as the dosimetric variation between planning and treatment is not affected by the respiratory cycle, while the 4DCT increases accuracy of delineation.[14]

SBRT techniques allow for a higher dose per fraction compared with 3DCRT or IMRT, by using accurate imaging practices and superior stabilisation equipment. A hyper-fractionated dose of 60 Gy in three fractions is used, giving a biological equivalent dose of 100 Gy, significantly improving local control. SBRT is limited by the shortfalls of target volume outlining, highlighting the need for faster and more reliable delineation methods. It is unlikely SBRT can be used for latter-stage disease due to requirements of smaller treatment volumes.[11] 30% of NSCLC patients are stage 4 at the time of diagnosis, indicating the need to adopt optimal planning and treatment regimes for early stage disease.[13]

This systematic literature review aims to compare the wide variety of planning methods in the current evidence base in order to determine the optimal technique for 4DCT planning of NSCLC.

METHODS

The purpose of this review was to establish the optimal technique for PTV definition and treatment of NSCLC. Literature reviewed was located predominantly via ScienceDirect and EBSCO Host databases such as PubMed and Medline. Papers were located that satisfied a range of criteria: related to a diagnosis of NSCLC, published within 10 years and focused on treatment planning methods. Papers with poor reliability were rejected.

DISCUSSION

Delineation methods

The delineation of target volumes for NSCLC patients is problematic due to the extent of motion experienced throughout the breathing cycle. Various methods can account for this, such as MIP, AI end-of-expiration (EOE), end-of-inspiration (EOI) and ten-phase overlap approaches.[2] The ten-phase overlap approach delineates the target in each phase of the breathing cycle individually. This is clinically unsuitable as it can take ~2·5 hours to perform.[10] Table 1 summarises the relative advantages and disadvantages of the different delineation methods.

Bradley et al.[9] noted that for stage 1 NSCLC, MIP was more reliable than either AI or the

Table 1. Delineation methods within literature

Source	Delineation	Stage of disease	Results	Notes
Bradley et al. 2006	MIP versus AI standard	1	MIP more reliable than AI	Unable to calculate electron densities
Muirhead et al. 2008	MIP versus ten-phase overlap	1–3	MIP for stage 1 faster than ten-phase overlap; same accuracy.	Underestimate stage 2–3 disease
Reitz et al. 2009	MIP versus AI (IMRT)	1–3	MIP superior to AI	Requires visual confirmation
De Ruysscher et al. 2012	4D-PET-MIP	na	4D-PET-MIP more reliable than PET/CT is to 4D-CT-MIP	4D-PET ten-phase sum equivalent in volumes to 4D-PET-MIP

Abbreviations: MIP, maximum intensity projection; AI, average intensity; IMRT, intensity modulated radiation therapy; 4D-PET-MIP, four-dimensional positron emission tomography maximum intensity projection; 4D-CT-MIP, four-dimensional computed tomography maximum intensity projection.

common 3D helical scan delineation types. However, it was noted that the accuracy of dosimetric calculations on MIP datasets is inferior to that of AI, as electron densities cannot be recorded. As such, MIP can be used to identify target position, whereas AI is required to represent the dosimetric outcomes of the patient's treatment accurately.

This was supported further by Muirhead et al.,[10] who found that MIPs performed on stage 1 patients were similar to that of the common ten-phase overlap approach, and thus should be used to decrease planning time. However, the study also showed that stage 2–3 disease resulted in MIP datasets to underestimate the target volumes. In this case MIP cannot distinguish boundaries between tissues with similar or higher Hounsfield Units, and therefore erroneously rejects these voxels.

Reitz et al.[2] contradicted both these studies, when reviewing IMRT planning of NSCLC patients in all four stages of disease. The authors concluded that MIP was superior to that of AI as it delineated smaller margins. However, the study consisted of only five patients, three of whom were stage 1. Larger scale study findings would be required to refute the other studies. Muirhead et al.,[10] noted that smaller margins created by the MIP were of concern, as volumes were not covered in all ten phases, thus signifying both a need for larger case size and for visual confirmation to check coverage of the entire breathing cycle.

It has been illustrated that positron emission tomography (PET) has improved the staging and treatment of NSCLC patients.[15] Recently, Callahan et al.[16] demonstrated how 4D-PET-MIP utilises the existing MIP technology and applies it to PET scans for the same purposes as used in CT. It was found that 4D-PET enabled more accurate positioning of target volumes in the scans of nine patients. The edges of the volumes were more defined, as was the overall position. The use of MIP to delineate the targets was found to be as accurate as the ten-phase overlap technique. Importantly, PET scans are more reliable near soft tissue structures, such as peripheral tumour placements, as the soft-tissue contrast is greater than in the CT-MIP technique. These findings were supported by a 2012 study[17] which concluded that 3D-PET did not accurately match 4D-CT-MIP delineations. Further investigations into the use of 4D-PET-MIP should be considered.

Overall, MIP proves an efficient method of delineating early stage target volumes. The drawbacks relating to dosimetric properties and accuracy during the latter stages of disease prove to be significant enough to warrant either the continued use of ten-phase overlap delineations, or an alternative method.

FB

Liu et al.[18] studied 152 patients of stage 2 and three NSCLC, in order to assess the 3D motion of target volumes. About 77% of patients did not receive surgery before planning and treatment, and 60–70% had lesions located within the central region. The motion detection in three dimensions was investigated as the authors

Table 2. Free-breathing planning and treatment methods within literature

Source	Stage	Case size	Delineation method	Results
Liu et al, 2007	2–4	152	EOE	Lesions in lower lobes and early stage disease prove most mobile
Fritz et al. 2008	1	40	EOE, EOI and mid-ventilation	81% control rate at 3 years
Li et al. 2011		28	3D versus 4D	Reduction in PTV size and normal tissue dose; increase in planning time; individualised margins cover PTV more accurately
Starkschall et al. 2009	3	15	EOE and deformable image registration	4D scans allow for reduction in PTV
Reitz et al. 2009	1–4	5	MIP and AI	MIP optimal target delineation method

Abbreviations: EOE, end-of-expiration; EOI, end-of-inspiration; PTV, planning target volume; MIP, maximum intensity projection; AI, average intensity.

noted sufficient literature stating target volume motion in the lung is anisotropic, disproving the use of universal margins. The breathing regularities of the patient, tumour size and location are directly linked to the degree of motion the target experiences (Table 2).

Using EOE GTV delineation, FB 4DCT scans were monitored by Varian's RPM technology. The infrared markers on the abdomen allowed the system to track the breathing cycle effectively, measuring ten phases across the cycle. Visual verification was required once the rigid body deformation technique was applied to the fusion of the GTV phases. This allowed for the PTV to accommodate for tumour motion in each phase. The results showed a higher frequency of motion in the superior and inferior directions, and lower lobe lesions moved most often due to close proximity to the diaphragm. Additionally the smaller lesions were proved to move more than larger and superior lesions; this was linked to the effect of the diaphragm motion.

The report's findings were strengthened as it had the most significant sample size of the articles reviewed; 152 patients with 166 tumours made for reliable findings. It also reinforced the claims made by the authors of the effect and dependency of target motion according to anatomical and disease-specific characteristics. The position and motion of the targets is clearly relevant to the planning of many lung tumours. Many of the patients were of stage 3 or 4 NSCLC, whereas stage 1 and 2 are the most likely to have significant motion. A greater range of patient types could increase the validity of the results, to avoid skewing of results from the latter stages of the disease. Additionally, results could be separated into early and late stage disease. Future studies should investigate planning time, staff numbers and workflow changes required, as well as cost of technology and systems. Expected control and survival rates should also be compared with conventional methods of lung treatments.

Fritz et al.[19] performed a study of single-dose fractionation of 40 stage 1 NSCLC patients that aimed to measure the side effects, control rates, survival rates and overall success associated with 4DCT and single-dose treatments. The authors found 4DCT to be more accurate than 3DCT for PTV delineation. Furthermore, accounting for motion in FB planning scans decreased cost compared with gated treatments, as no extra technology is required to be installed in the treatment area. The planning was performed through the use of three scans; EOI, EOE and mid ventilation. The combination of these three scans allowed for a projection of the extent of target motion during the breathing cycle.[7] A 10–15 mm margin was placed on the GTV. The results included 81% control rate at 3 years, with overall survival for 2 and 3 years at 66% and 53%, respectively. The cancer specific survival was 71% and 57% for 2 and 3 years post-treatment, respectively. The side effects to patients included a 75% rate of radiation pneumonitis, with no other significant toxicities or side effects. The strengths of this report include a significant patient sample size ($n = 40$), with similar type and stage of disease; excellent

for result comparison. The target volume size was quite variable, which illustrated the abilities of the 4DCT and planning system to be applied to a variation of tumours. Patient follow up was also extensive and ongoing. The reporting of this data is critical when using IMRT where long-term effects are still to be determined. The use of 4DCT for single-fraction treatment of stage 1 NSCLC has not been reported elsewhere at the time of this review, therefore it is difficult to draw comparative conclusions.

Li et al.[20] performed a study on 28 NSCLC patients, in an attempt to calculate the positional and volumetric differences of 3DCT and 4DCT planning methods. Three PTV's were created during the planning, one each for the different scan type and an additional one to measure the vector difference. The authors found that 4DCT planning has the potential to decrease the risk of target miss during treatment and normal tissue irradiation, by increasing the accuracy of margins for the patient. Using an individualised technique is superior as the motion of the target is accounted for, rather than a universal margin to encompass 'possible' motion.

The patients were grouped depending on the stage of their disease and location of the lesion. Varian's RPM system was used to monitor breathing cycles of patients, 'binning' ten phases of the scan. The physicians delineated the target volumes on the base slice of 50%, or end expiration. The results showed a 25–48% reduction of PTV size and a 30·8–48·4% decrease in normal tissue dose using 4DCT. The planning time for 4DCT was higher than that of 3DCT methods: 28 ± 15 minutes compared with 5–10 minutes, for GTV delineation. The report concluded that individualised margins are able to cover the majority of 4D target volumes; however this usually results in over-irradiating normal tissue. The study noted that to do this using 4DCT increases the workload of planning systems and patient exposure. Irregular breathing patterns of patients can also negate some of the benefits of 4D systems and a need for coaching or gated methods would be required. This can be problematic for NSCLC patients as the age and co-morbidities often found in patients can have significant effects on the breathing patterns.

The strengths of this paper are the comparable results over a wide variety of patient stages and pathologies. The position of the lesions, the stage of the disease and the multiple PTV delineations allowed for an extensive collation of data. The variations of motion in all three dimensions and the positional differences of lesions are also important to show the effects of 4DCT planning for the different presentations of disease.

Starkschall et al.[21] measured the differences between dose distributions and calculations of 3D and 4D CT planning systems for 15 NSCLC stage three patients. CT was combined with monitoring devices to form a 4D planning system, depicting ten phases of respiration. Deformable image registration was used on each of the ten phases, overlaying the EOE CTV volume over the nine other phases, in order to calculate an average dose distribution throughout the full motion of the target. The authors noted only a small increase in actual planning time, yet a significant increase in dose calculations, as there were ten datasets for the 4DCT compared with one for 3DCT. 4DCT PTV delineation resulted in an average reduction of 1·7% of volume compared with 3DCT. This illustrates the increased accuracy of the 4D scans, as there was an additional 1 mm margin added to the 3D scans for uncertainty. The strengths of this paper include the variability of target volume size and the use of deformable registration techniques, rather than rigid body methods. Rigid body is limited by approximations of the effect of motion, whereas the planning technique used in this study is similar to adaptive planning. The report was limited by the small case size ($n = 15$) and the use of 3D planning techniques in a 4D system. Although 4DCT was used, the custom 4D planning was effectively a copy of 3D methods transferred across using 4DCT-delineated volumes. The differences and limitations of gating methods compared with the 4DCT plan and the associated outcomes should be further investigated, as well as the effect of respiratory changes through treatment and the impact of those on

Table 3. Gated planning and treatment methods within literature

Source	Stage	Case size	Delineation method	Results
Underberg et al. 2005	1	31	Isotropic margins + ITV	30% PTV reduction for 38%; 50% reduction for 15%.
van der Voort van Zyp et al. 2009	1–2	70	na	2-year survival at 96% and 78%; T-1 disease higher survival rates

Abbreviations: ITV, internal target volume; PTV, planning target volume.

the dose distribution results. By performing a 4D plan (i.e., using a 4D planning system) a more accurate representation of results could be provided. Control and survival rates would also be useful.

Reitz et al.[2] studied the use of simple IMRT for the planning of five NSCLC patients, ranging from stage 1–4 disease. Using FB 4DCT, the aim of the study was to quantify the feasibility of using five-field IMRT for NSCLC. The 4DCT scan was performed with an Anzai belt to monitor respiration during the scan. Target delineation was performed using maximum intensity (MIP) or mean intensity (MI or AI) methods.

The authors note that using EOE or EOI proves less accurate as it fails to account for ant-post and left-right deviations. It is unrealistic to perform delineations on ten phases of a patient's breathing cycle, due to time constraints in the clinical setting. Delineation using MIP proved more accurate and enabled margin reduction compared with that of AI plans. The margins for MIP plans were 0·8 cm while AI used a 1·5 cm margin.

The strengths of this report include the standard beam arrangement, dose tolerances and the use of tables and illustrations to concisely depict the gain of using MIP delineation over AI. The use of geometric equivalent uniform dose and TCP tabled information was beneficial, and proved one of the only pieces of literature to quantify the probabilities of the planning outcomes.

The limitations of MIP include total lung volume representation similar to that of EOE scans, not indicative of the actual lung volume during treatment. This provides far less lung volume during most of the treatment cycle (during FB). Additionally, electron densities cannot be gained from the MIP image, therefore using the AI data was required for both total volume calculations and accurate dosimetric readings.

Gating and tracking

Gated methods in combination with 4DCT scans provide more accurate alternatives to conventional 3DCRT planning of NSCLC. Commonly, a FB 4DCT is used to visualise the full extent of motion across the breathing cycle, and to use the most stable region of this cycle for treatment purposes. Treatments are delivered using either a breath-hold technique or FB, where the beam-on of the machine occurs at pre-determined stages of the respiratory cycle.[5,22] There are two approaches to gated treatments, where the breathing cycle is monitored by internal or external means. Internal gating requires invasive procedures for patients who are frequently unfit for such procedures. External gating can be performed using detection devices on the abdomen, spirometers and tracing methods.[22] Over 90% of lung patients can use external systems to achieve gating, compared with a significantly lower proportion for internal.[8] Table 3 summarises the studies relating to gated techniques.

The use of IMRT-gated treatments for NSCLC can increase treatment times by as much as 10 minutes.[8] This is due to the beam-on time representing only 20% of the respiratory cycle, at the most stable point, usually end-expiration.[23] Calculation and planning can be 15 times longer than the 3DCRT and non-gated approaches. With increased time, there is a risk the reduced patient comfort can cause movement. It is possible that cell-repair within the target may be possible when treatments such as

stereotactic can reach 3 hours for a single treatment, with an average of 100 minutes. This raises questions as to the validity of such gated treatments if the time taken to accurately position, image and treat according to the breathing cycle can have a negative effect on the patient's quality of life.[8]

Underberg et al.[22] investigated the use of gated 4DCT planning and treatment for 31 stage 1 NSCLC patients. The aim of the study was to investigate the benefits of using isotropic margins and devising a method of future patient selection. A FB 4DCT scan was performed, using the Varian RPM device as a means to bin ten phases of the respiratory cycle. The extent of motion was observed from the maximum displacements on the 3D datasets. The ITVs included all phases of delineated GTV, therefore accounting for all motion. Isotropic margins were added to all three ITV's (10 mm, 3 mm, gating with 3 mm) to form variable PTVs for comparison. Eight to 12 non-coplanar beams were used for the dosimetry process; three separate fractionation schedules were used to view possible benefits for hypo-fractionated treatments. The report concluded that gating offered a 30% reduction of PTVs for 38% of targets and 50% in 15% of targets. The conclusions of this article were strengthened by an appropriate sample size and the patient selection methods. The reduction of margins illustrated by the normal tissue dose regions was effective.

It would be interesting to determine the impact of the technology on patient quality of life measures, such as side effects, control rates and survival rates as well as related costs, ease of use, staff and workflow requirements of RPM as well as impact on workload. The use of isotropic over individualised margins should be investigated further as literature has shown the latter to be more accurate.

A 2009 study investigated the use of SBRT using repeat scans and real-time tracking devices.[3] Using a breath-hold technique for the scanning of patients, repeat scans were used to confirm positioning of the markers inserted into the patient. Out of 70 patients with T-1 or T-2 stage NSCLC, two groups were formed: 59 received 60 Gy while the remainder received 45 Gy over three fractions. The control rate after 2 years was 96% and 78% accordingly, with overall survival at 62% and cause specific survival at 85%. Grade 3 toxicity was only experienced in 10% of patients. It was noted that the control rates were higher for those with T-1 disease, due to lower local recurrence risk and smaller target volumes. The paper highlighted the quality of life results, which has been overlooked in other literature. Control rates at 2 years proved high and in line with similar studies noted in the literature.

CONCLUSION

This review demonstrated that passive techniques are effective for planning NSCLC treatments. It has been shown that 4DCT out-performs 3DCT when accounting for organ motion during planning, leading to margin reductions and a more accurate and individualised delineation process. Various methods of PTV definition have been identified, with stage-specific recommendations formed. Briefly, the literature supported SBRT and IMRT for early and late stage disease treatment, respectively.

The use of MIP delineation is insufficient for latter stage disease. This effect could be more pronounced when irregular breathing patterns are prominent, where deviations from planning position can be as high as 8 mm. To reduce these irregularities abdominal compression and breath-coaching could improve accuracy. Overlaying MIP-ITV on each scan and adjusting to ensure coverage allows a quick delineation process, without the drawback of volume underestimation. This is slower than MIP as a sole modality, but quicker than the ten-phase delineation approach. Daily imaging such as cone-beam computed tomography matching should be performed before treatment, especially in the use of IMRT or SBRT for more precise positioning. It would be interesting to see evaluation of more 4D-PET delineation techniques in future studies to determine the optimal technique for PTV delineation.

The review highlighted several limitations of the evidence base and future studies would

benefit from more standardised measures in order to increase the fluidity of comparison between papers. Some remaining questions concern differences in planning time between 4D and 3D, comparison of gating and FB efficacy and comparison of delineation times. The cost of the technologies used, in-house programs, and the education for staff and patients required to work effectively within the department should also be established. Quality of life data at 5 years needs to be reported for such work to illustrate the true benefits of techniques.

Separating early stage and late stage disease could avoid skewing of data within reports. The discussion of dose tolerances, planning time between technologies, costs of systems and overall departmental efficiency would highlight feasibility of techniques.

Currently, 3DCRT has reached its limit in the effectiveness of treating NSCLC. New technologies such as IMRT are more commonly used in departments to improve the quality of treatment. Although gating and SBRT have shown improvements for early stage disease, it is more likely that FB IMRT will be implemented in departments due to low cost and minimal workload changes required. FB IMRT using a MIP-visual confirmation delineation technique allows for a superior NSCLC treatment than 3DCRT.

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Conflicts of Interest

None.

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